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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,497	12/12/2005	Lars Terje Holmaas	PN0324	4578
36335 7590 05/27/2009 GE HEALTHCARE, INC. IP DEPARTMENT 101 CARNEGIE CENTER PRINCETON, NJ 08540-6231				
EXAMINER KATAKAM, SUDHAKAR				
ART UNIT 1621		PAPER NUMBER		
MAIL DATE 05/27/2009		DELIVERY MODE PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.



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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 10/560,497  
Filing Date: December 12, 2005  
Appellant(s): HOLMAAS ET AL.

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Craig M. Bohlken  
For Appellant

This is in response to the appeal brief filed 3<sup>rd</sup> April 2009 appealing from the Office  
action mailed 9<sup>th</sup> Oct 2009.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

A substantially correct copy of appealed claim 1-20 appears on pages 9-11 of the Appendix to the appellant's brief. The minor errors are as follows: claims are improperly numbered.

**(8) Evidence Relied Upon**

5,948,940

Malthe-Sorensen

9-1999

### (9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

#### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Malthe-Sorensen et al** (US 5,948,940).

**Malthe-Sorensen et al** teach a process for the production of iohexol, said process comprising reacting 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide with a 2,3-dihydroxypropylating agent in the presence of a base and a solvent, viz., **2-methoxy-ethanol** (col 2, lines 1-7) which is a C<sub>1</sub>-C<sub>5</sub>-monoalkylether of a C<sub>2</sub>-C<sub>10</sub> alkylene-glycol. The example shows that the solvent, viz., 2-methoxy-ethanol (278 ml) per 283g of 5-acetamide (see example 1). It also teaches

the purification of crude iohexol using **2-methoxy-ethanol**, which is a C<sub>1</sub>-C<sub>5</sub>-monoalkylether of a C<sub>2</sub>-C<sub>10</sub> alkylene-glycol, as solvent and isopropanol, which is a C<sub>1</sub>-C<sub>4</sub> alkanol, as a co-solvent. The crude iohexol purified preferably by recrystallization using the isopropanol (see col.3, lines 8-40).

The difference between the instant invention and **Malthe-Sorensen et al** is that the instant invention used the **1-methoxy-2-propanol**, whereas the reference used **2-methoxy-ethanol**.

It would have been obvious to a person of ordinary skill in the art, at the time of present invention was made, to have modified the reference's teachings by using an alternative solvent, such as **1-methoxy-2-propanol** with a reasonable expectation of success. The solvents differ by one carbon. Please note that adjacent homologs are considered to be obvious absent unexpected results. In re Henze, 85 USPQ 261, 263, CCPA 1950.

#### **(10) Response to Argument**

The examiner acknowledges applicants argument that **Malthe-Sorensen** does not teach, describe or suggest using any other solvent other than 2-methoxy-ethanol.

The examiner, however, contends that **Malthe-Sorensen** clearly suggested to one having ordinary skill in the art the use of similar solvents. The solvents differ by a methyl group to the solvent used in the prior art for making iohexol and, therefore, these solvents are considered as adjacent homologs, and expect to have similar properties.

The adjacent homologs are considered to be obvious absent unexpected results. In re Henze, 85 USPQ 261, 263, CCPA 1950.

The examiner acknowledges applicants' argument that their solvent, viz., 1-methoxy-2-propanol, is very different from 2-methoxy-ethanol in the manufacture of iohexol.

The examiner, however, contends that the results shown by applicants in tables 1 and 2 [Remarks filed on 2/28/08], such as yield/purity of the product and the amount of other impurities, are not significantly different from the closest prior art. Please note that the ratio of amount of NaOH added to the reactants is different compared to the ratio mentioned in the example 1 of prior art. Also the ratios of different reactants used in the instant application are different from the prior art. This difference may cause slight difference in the purity and yield of the product, since applicants did not show real side by side comparison with the closest prior art. Are these differences due to the different ratios of the reactants or to the solvents differing by a methyl group? Applicants' showings are also not commensurate with the scope of the claims, since applicants show only one compound in the specification, but claim large number of solvents and co-solvents.

The examiner acknowledges applicants argument that **Malthe-Sorensen** does describe using 2-methoxy-ethanol as a solvent in both the alkylation and in the purification step, however, the solvent mixture only comprises a very small amount of 2-methoxy-ethanol in the purification step.

The examiner, however, contends that varying the concentration ratios of solvents is optimizable parameters and a routine practice for a given process. Absent any showing of unusual and/or unexpected results over the applicants' particular concentration of solvent in the process, the claim is deemed to be obvious.

With regard to the WO 02/083623, **Malthe-Sorensen** also showed the use of co-solvents in the preparation of iohexol.

With regard to applicants Declaration, applicants need to show the advantage of their solvent over the solvent of cited prior art in a side by side comparison. Absent any showing of unusual and/or unexpected results over the applicants' solvent in the process, the claim is deemed to be obvious.

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Sudhakar Katakam/

Patent Examiner

Conferees:

/Peter G O'Sullivan/

Primary Examiner, Art Unit 1621

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Art Unit: 1621

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